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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,131	09/26/2006	Audrey Royere	0512-1347	7355

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EXAMINER	
CRAIGO, WILLIAM A	
ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
04/12/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DocketingDept@young-thompson.com

Office Action Summary	Application No.	Applicant(s)	
	10/591,131	ROYERE ET AL.	
	Examiner	Art Unit	
	WILLIAM CRAIGO	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-33,35-38 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-33, 35-38 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 22 December, 2010 has been entered.

Status of the Claims

Acknowledgment is made of the response filed 22 December, 2010. In that paper, claim 21 was amended, no claims were cancelled, no claims were added. Claims 21-33, 35-38 and 40 are treated on the merits in this action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 21-33, 35, 36, 38, 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Laakso, WO 99/20253 in view of Lobo, US 5589322 A and Leal Calderon, US 6602917 B1.

Laasko is directed to methods of encapsulation of active substances in a biodegradable polymer (abstract). Laasko, example 1, describes a process for preparing microspheres by preparing a single emulsion comprising an organic phase (ethyl acetate) a pharmaceutically active ingredient (BSA, protein) and a biodegradable polymer dissolved in an organic solvent. Laasko describes vortex mixing and stirring. Laasko describes stirring overnight meeting the limitation of removing the solvent form the organic phase of the single emulsion obtained in step b) to obtain microspheres. Laasko describes filtering the suspension to isolate the microspheres meeting the limitation of isolating the microspheres so obtained.

As the microspheres are constituted of PLGA, the microspheres described in Laasko meet the limitation of wherein the microspheres are constituted in majority by

the biodegradable polymer (instant claim 22). PLGA meets the limitations of instant claims 23 and 24. Ethyl acetate meets the limitations of instant claim 26. BSA meets the limitation of peptide or protein as recited in instant claim 29. Laasko, example 1, describes an emulsion containing 0.47g PLGA in 3mL ethyl acetate (d = 0.897 g/mL). (3 mL x 0.897 g/mL = 2.691g ethyl acetate). % polymer = ((0.47)/(0.47+2.691) x 100 %) = 14.86 % meeting the limitation of instant claim 32. Laasko, example 1 describes an emulsion containing 0.044 g of BSA; the organic phase is (2.691 g ethyl acetate + 0.47 g polymer = 3.16 g); 0.044g / 3.16g x 100% = 1.39 % of the pharmaceutically active ingredient meeting the limitations of instant claim 33. Laasko describes stabilizing agents such as polyvinyl alcohol (example 2) and viscosity agents (example 1 discloses water as a viscosity reducing agent) meeting the limitations of instant claims 35 and 36. The microsphere encapsulation method of Laasko describes a method whereby the organic phase is carried out by extraction of water because the ethyl acetate appears to be extracted into the water by adding an excess of water whereby the dispersed ethyl acetate is extracted into the water and allowed to evaporate meeting the limitations of instant claim 38. Laasko, claim 15 describes biologically active substances including antibiotics, anti-inflammatory agents, antihistamines, anti-allergeics, sedatives, among other agents, meeting the limitations of instant claim 40. Laasko, pg. 11, lines 15-18 teaches polymers with molecular weights of 2000 to 200000, suggesting the limitations of instant claim 25. Laasko, pg. 10 teaches classes of therapeutic drugs including anti-tumor agents, antibiotics antidepressants and steroids. Laasko, pg, 10, line 33- pg 11 line 7 teaches drugs containing amines and carboxylates which can be used as salts or

"per se" (i.e. free base or carboxylic acid). Drugs containing these groups can be made lipophilic and lipid soluble (i.e. uncharged) or salt forms, water soluble (i.e. charged) suggesting the limitations of instant claims 27 and 28. Laasko, pg 9 teaches protein drugs such as insulin; a protein is comprised of hydrophilic active ingredients in combination with lipophilic active ingredients because proteins are made up of amino acids some of which are hydrophilic, for example arginine, and some are lipophilic, for example phenylalanine. Since amino acids are active ingredients in and of themselves and proteins are combined amino acids the proteins taught in Laasko meet the limitation of a hydrophilic active ingredient in combination with a lipophilic active ingredient as recited in instant claim 30. Laasko teaches a 40% (w/w) solution of polyethylene glycol suggesting the limitation of wherein the organic phase of the emulsion represents from 10 to 60% by weight relative to the total weight of the emulsion as in instant claim 31.

While Laasko does not expressly describe the viscosity ratio of the organic phase and the aqueous phase, controlling the viscosity in the processing of emulsions to prepare microspheres is known and conventional as taught in Lobo.

Lobo teaches the viscosity ratio of the aqueous phase relative to the liquid organic phase has been found to affect dispersion particle size (see Lobo, Col. 2, lines 43-67). Generally as the ratio of the organic phase viscosity to the aqueous phase viscosity at the temperature of homogenization) is decreased, smaller dispersion particle sizes are achieved. Lobo, (examples 1-3) teaches viscosity ratios, q, listed in the tables between 0.1 and 10 as claimed.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the known technique of controlling the viscosity ratio between the organic and aqueous phases as taught by Lobo to improve the emulsion methods as taught in Laasko in the same way because Laasko describes an emulsion method to prepare microspheres, Lobo teaches particle sizes produced using emulsion techniques can be controlled by controlling the viscosity ratio of the organic phase and the aqueous phase; thus the skilled artisan would have predicted the technique of controlling the viscosity ratio of organic phase and aqueous phase would have been useful for controlling the particle size in other emulsion methods. Lobo provides evidence that controlling the viscosity ratio as claimed had been made part of the ordinary capabilities of one skilled in the art based upon the teaching of such an improvement in similar emulsion processes.

While neither Laasko nor Lobo expressly teach mixing is accomplished by controlled laminar shear, however, methods of preparing emulsions using controlled laminar shear were known in the art.

Leal Calderon is directed to processes for providing a stable emulsion by emulsifying a first hydrophobic or hydrophilic phase by mixing together the first phase and the second phase under a laminar shear regime (abstract). From Leal Calderon, the skilled artisan is taught: laminar shear is preferred for forming emulsions because the emulsion can be formed under low shear very quickly (col. 2, lines 5-9), provides emulsions with very narrow particle size distributions and the average diameter of the droplets can be readily controlled (col. 3, lines 43-49); the shear rate should be

controlled (example 3 teaches stirring speed should not exceed a threshold value of 1000 rpm, above which the excessively violent shear destroys the concentrated emulsion); controlled laminar shear is expressly suggested for preparing emulsions of hydrophobic or hydrophilic phase including therapeutic, cosmetic or food-use interest (col. 6, lines 17-21), suggesting lipid soluble active ingredients and water soluble active ingredients as in instant claims 27 and 28.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the known technique of controlled laminar shear to improve similar emulsion methods in the same way. Laasko teaches an emulsification method for producing microspheres comprising a single emulsion, an organic phase comprising a pharmaceutically active ingredient, biodegradable polymer dissolved in the organic solvent and at least one aqueous phase. Lobo teaches controlling the ratio of the viscosity of the organic phase and the aqueous phase as claimed to control the particle size in an emulsion. Leal Calderon teaches forming the emulsion through controlled laminar shear reduces the time needed to form the emulsion and provides the emulsion with an extremely narrow particle size distribution (i.e. monodisperse particles). The combined teachings support a finding that one of ordinary skill would have been motivated to apply the teachings of Lobo and Leal Calderon to known methods of fabricating microspheres and the results would have been predictable.

Accordingly, the subject matter of instant claims 21-33, 35, 36, 38, 40 would have been prima facie obvious to one of ordinary skill at the time the invention was made, particularly in the absence of evidence to the contrary.

Claims 31 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Laakso, WO 99/20253 in view of Lobo, US 5589322 A and Leal Calderon, US 6602917 B1 as applied to claims 21-33, 35, 36, 38, 40 above, and further in view of Bibette, US 5938581 A.

The teachings of Laasko, Lobo and Leal Calderon are discussed above. The combined teachings are silent to the use of a Couette device. However such devices were known in the art to provide emulsions.

Bibette is directed to emulsion manufacturing processes. Bibette teaches the use of a Couette device (Fig. 1, col. 5, lines 45-55, example 9) for providing an emulsion consisting of 60% by weight of liquid petrolatum (organic phase) in water. Bibette teaches the use of Couette devices can be used to produce emulsions with a controlled shear rate.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use a Couette device as instantly claimed to provide an emulsion for preparing microspheres as described by Laasko, Lobo and Leal Calderon with a reasonable expectation of success. Laasko teaches an emulsification method for producing microspheres comprising a single emulsion, an organic phase comprising a pharmaceutically active ingredient, biodegradable polymer dissolved in the organic solvent and at least one aqueous phase. Lobo teaches controlling the ratio of the viscosity of the organic phase and the aqueous phase as claimed to control the particle size in an emulsion. Leal Calderon teaches forming the emulsion through controlled laminar shear reduces the time needed to form the emulsion and provides the emulsion

with an extremely narrow particle size distribution (i.e. monodisperse particles). Bibette teaches a Couette device for providing an emulsion allows control of the shear rate; the skilled artisan is taught by Leal Calderon to control the shear rate for providing extremely narrow particle size distributions (i.e. monodisperse particles).

Accordingly, the subject matter of instant claims 31 and 37 would have been prima facie obvious to one of ordinary skill at the time the invention was made, particularly in the absence of evidence to the contrary.

Response to Arguments

Applicant's arguments with respect to claims 21-33, 35-38 and 40 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to WILLIAM CRAIGO whose telephone number is (571)270-1347. The examiner can normally be reached on Monday - Friday, 7:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/WILLIAM CRAIGO/
Examiner, Art Unit 1615

/Leon B Lankford/
Primary Examiner, Art Unit 1651